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Thromboelastography to direct the administration of recombinant activated factor VII in a child with traumatic injury requiring massive transfusion*

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Objective: **To describe the use of thromboelastography (TEG) to direct hemostatic resuscitation in a child with traumatic injury requiring massive transfusion.**

Design: **Case report.**

Setting: **Level 1 pediatric trauma center in an academic tertiary care facility.**

Patient: **A 5-year-old boy with grade IV liver injury and right common hepatic artery laceration.**

Intervention: **TEG-directed resuscitation, including recombinant activated factor VII.**

Measurements and Main Results: **Measurements included vital signs, laboratory results to include TEG values, and blood product administration. TEG-directed resuscitation with recombinant activated factor VII was associated with the prevention of increased intracranial hemorrhage and survival in a coagulopathic patient with a life-threatening traumatic injury.**

Conclusion: **Our clinical and TEG laboratory results postresuscitation support the potential use of TEG as a tool to direct hemostatic resuscitation in patients with severe trauma requiring massive transfusion. TEG is a quick and focused method of qualitatively assessing the entire coagulation cascade, from clot formation to fibrinolysis that permits a targeted transfusion approach to the treatment of coagulopathy. TEG has the potential to rapidly and effectively direct hemostatic resuscitation in patients with the coagulopathy of trauma. (Pediatr Crit Care Med 2009; 10: e22–e26)**

KEY WORDS: thromboelastography; coagulopathy; trauma; children; recombinant activated factor VII

In the United States, hemorrhage is the primary cause of death in 40% to 60% of traumatic injuries (1), and the leading cause of death in children (2). The coagulopathy of trauma that is associated with severity of injury is a process that is well described (3). Massive transfusion, defined as ≥10 units of red blood cells (RBCs) in 24 hours for adults correlates to ~50 mL/kg of RBCs in 24 hours in children, although in children this is not clearly defined. Both coagulopathy and massive transfusion have been independently associated with an increased risk of mortality in patients with traumatic injuries (3, 4).

Hemostatic or damage control resuscitation is an emerging concept that has been applied to the management of severe trauma patients who present with or develop a coagulopathy (5). It includes rapid surgical control of bleeding, with aggressive treatment of coagulopathy, with a 1:1:1 unit ratio of plasma: RBCs: platelets, and the early use of cryoprecipitate and recombinant activated factor VII (rFVIIa), while simultaneously minimizing the use of products that exacerbate dilutional coagulopathy such as excessive crystalloid and RBC transfusions. Massive transfusion is associated with high mortality: more than 60% of these patients die within 6 hours of admission (6). Rapid and aggressive treatment of the coagulopathy of trauma improves survival (8, 9).

A laboratory method that may be a helpful adjunct to perform targeted hemostatic resuscitation is thromboelastography (TEG). TEG is a rapid point-of-care test that qualitatively measures the entire coagulation cascade, including fibrinolysis, in whole blood (10–12). This case report describes the use of TEG to direct hemostatic resuscitation, including the administration of rFVIIa, in a child with traumatic injury who required massive transfusion.

CASE REPORT

The institutional review board was consulted; it approved the following case report and waived the need for consent. A 5-year-old, 24 kg, Hispanic male pedestrian was struck by a pickup truck. On arrival to Wilford Hall Trauma Center, the patient was unresponsive and in uncompensated hemorrhagic shock. Patient vital signs, laboratory values, TEG values, crystalloid amount, and blood products transfused are summarized according to hospital location and time in Table 1.

Initial evaluation in the trauma bay with focused abdominal sonogram for trauma revealed hepato-renal and splenorenal free fluid. Computerized tomography scans revealed a 1.1 × 1 cm left frontal cerebral intraparenchymal hemorrhage, a large right pulmonary contusion, a small left pulmonary contusion, a grade IV liver laceration, a spleen laceration, and free fluid in abdomen. On laparotomy, a grade IV liver injury with

*See also p. 274.

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Table 1. Thromboelastography results with vital signs, laboratory values, and products transfused according to time and location

Location	Trauma Bay	Radiology	OR		PICU	IR		PICU
Time	0030	0110	0150	0220	0320	0405	0505	0530
Vitals: HR (bpm)	160	139	155	158	178	190	150	152
SBP (mm Hg)	62/27	89/49	80/38	78/40	84/36	50/−	130/88	132/68
							← Coil embolidiztion	
Lab results: pH	7.32		7.35		7.25	7.21		7.35
$paCO_2$	28		32		39	41		40
paO_2	425		180		150	234		187
HCO_3^-	14		17		17	16		22
Deficit	−10		−7		−10	−11		−3
Lactate	4.9		5.8		4.4	5.8		5.1
Hb (g/dL)	11.4		11		11			11
PLT ($\times 10^3/mm^3$)	225		193		76			119
PT (11.3–14.5 sec)			25.4					12.7
PTT (25.3–35.9 sec)			33.2					39
FGN (mg/dL)			117					234
D-Dimer (units)			>20					3.6
TEG results: R-time (sec)			1.5					4.8
K-time (sec)			4.3					2.4
Alpha angle (°)			48					59
MA (mm)			44					55
Ly 30 (%)			0					0
G (dyne/cm^2)			4					6.1
Transfusion: RBC (mL)	800[a]		790			830		
FFP (mL)	245[b]		500			640		
aPLT (mL)			480 ordered→		Transfused			
Cryoprecipitate (U)			4 U ordered→		Transfused			
rFVIIa			2.4 mg			2.4 mg		
Normal saline (mL)	500	500	1500		75	75		440

OR, operating room; PICU, pediatric intensive care unit; IR, interventional radiology, HR, heart rate; SBP, systolic blood pressure; Hb, hemoglobin; PLT, platelet; PT, prothrombin time; PTT, partial thromboplastin time; FGN, fibrinogen; TEG, thromboelastography; RBC, red blood cell; FFP, fresh frozen plasma; aPLT, apheresed platelet; U, units; rFVIIa, recombinant activated factor VII.

[a]Indicates inclusion of 300 mL of RBCs transfused before transfer to Wilford Hall Trauma Center; [b]indicates prethawed plasma. From Ref. 23.

right common hepatic artery laceration was recognized. Hemostasis could not safely be obtained directly and was temporized by packing the abdominal cavity. During this procedure TEG (TEG 5000, software version 3, Hemoscope, Niles, IL) analysis was performed. Within 5 minutes of sampling, TEG results indicated an R-time of 1.5 minutes, low normal alpha angle of 48.0°, and prolonged K-time at 4.3 minutes. On the basis of these results and the severity of the injury, 2.4 mg (100 μg/kg) of rFVIIa was immediately given with 500 mL of fresh frozen plasma and 4 units of cryoprecipitate. When additional TEG results of maximum amplitude (MA) 44.1 mm (decreased), and G 4.0 dynes/cm^2 (decreased) were reported, 2 units of apheresed platelets were transfused (see Table 2 for description and interpretation of TEG values). Standard coagulation laboratory values (platelet concentration, international normalized ratio [INR], fibrinogen) were reported 50 minutes after TEG values.

Definitive hemostatic control was deferred to interventional radiology for coil embolization of the right common hepatic artery. In interventional radiology as a result of continuing abdominal hemorrhage another 2.4 mg (100 μg/kg) of rFVIIa was given with additional fresh frozen plasma. Immediately after embolization, a detectable blood pressure was obtained at 130/88 mm Hg and the heart rate decreased to 150 beats per minute.

On transfer to the pediatric intensive care unit, repeat TEG analysis revealed normal coagulation function (Table 1). The total amount of crystalloids and blood products given from injury to control of bleeding was 2560 mL of normal saline, 2420 mL (100 mL/kg) RBCs, 1385 mL plasma, 480 mL apheresed platelets, 4 units cryoprecipitate, and 4.8 mg rFVIIa.

Following massive resuscitation and embolization of the right common hepatic artery, the patient's metabolic acidosis and vital signs normalized within hours. Computed tomography revealed the size of both the intraparenchymal cerebral hematoma, and the pulmonary contusion remained stable 16 hours after the initial evaluation. The patient was hospitalized for 13 days and was then discharged. On follow-up examination 2 months postinjury, he had fully recovered without neurologic deficits.

DISCUSSION

TEG to direct the resuscitation of traumatic injuries in children has not been described previously in the literature. It is possible that the use of TEG facilitated the appropriate use of blood products, led to effective treatment of the coagulopathy, and minimized the risk of cerebral or pulmonary edema in this child with cerebral and pulmonary lesions. Despite the initial severe coagulopathy, the appropriate treatment of coagulopathy in our patient was evidenced by the normalization of TEG values postresuscitation, immediately upon direct control of a major vascular injury. TEG may also prevent the excessive use of blood products for patients with traumatic injuries as a result of more rapid cessation of bleeding. Utilization of TEG has been associated with decreased use of blood products for adults requiring cardiovascular surgery (10). This is important in critically ill children since increased use of RBCs has been associated with increased morbidity and mortality (13, 14).

Table 2. Description and interpretation of TEG values

Normal TEG Values	Definition	Representation	Interpretation
R-time[a] 4–8 min	Time from test initiation to AMP of 2 mm	Clotting factor activity (clot initiation or initial fibrin formation)	↓ Hypercoaguability or moderate hemodilution (30%) ↑ Factor deficiency, heparin effect, severe hemodilution (>50%)
K-time[a] 0.5–4 min	Time from AMP of 2–20 mm	Fibrin formation Interaction of factors and platelets (clot amplification)	↑ Hypofibrinogenemia factor or platelet deficiency
Alpha angle 47–74°	Slope of tracing from R-time to K-time	Fibrin formation Interaction of factors and platelets (clot amplification)	↓ Hypofibrinogenemia factor or platelet deficiency
MA 55–73 mm	Greatest vertical amplitude of TEG tracing	Clot strength and platelet function	↓ Platelet deficiency[b], or hypofibrinogenemia ↑ Hypercoaguability
Shear elastic modulus G-value 6–13 dyne/cm^2	Parametric measurement derived from amplitude	Overall measure of clot strength or firmness	↓ Hypocoaguable state ↑ Hypercoaguable state
Clot lysis 30 min (LY_{30}) 0–7.5%	% of AMP reduction 30 min after MA time	Clot stability and fibrinolysis	>7.5% suggests hyperfibrinolysis

AMP, amplitude, TEG, thromboelastography; MA, maximum amplitude; ↑ indicates elevated value; ↓ indicates decreased value.
[a]Normal results reported are for noncitrate kaolin activated samples; [b]platelet deficiency can be either qualitative or quantitative.

Compared with TEG, the standard approach to measuring the coagulation system in patients has several disadvantages. It takes longer to get PT or partial thromboplastin time, INR, platelet and fibrinogen concentrations results (30–60 minutes) than initial TEG parameters (10 minutes). Recently, with point of care testing, INR and PT can be determined within 2 minutes. PT and partial thromboplastin time only evaluate partial aspects of the coagulation cascade, and since these standard tests are performed with plasma, the interaction between coagulation factors and platelets cannot be assessed. In addition, fibrinogen and platelet function cannot be measured rapidly with standard testing as is possible with TEG.

TEG may be able to guide appropriate dosing of rFVIIa (15) and may provide more accurate measurements of rFVIIa efficacy than PT. Since rFVIIa directly corrects PT *in vitro*, it is a poor indicator of *in vivo* hemostasis or efficacy if PT normalizes with rFVIIa use (16). However, correction of kaolin-activated TEG parameters with rFVIIa indicates *in vivo* efficacy (16). Future studies are needed to evaluate the role of TEG to direct rFVIIa use for patients with severe trauma who require rapid correction or treatment of the coagulopathy of trauma.

The principles and clinical applications of TEG have been reviewed previously (10–12, 17, 18). TEG was first utilized to describe the coagulopathy of trauma in 1969 (19). Its use in trauma has become more popular in recent years as it has been found to be quick and simple, and because it provides a broad functional evaluation of the entire coagulation process (12, 20–22). Parameters of a TEG tracing include R-time, K-time, alpha angle, MA, shear elastic modulus (G-value), and lysis at 30 minutes (Fig. 1). Normal values for kaolin-activated samples are described in Table 2. The effects of the activator being used is very important for the users of TEG to understand and the interpretation of TEG values must be done according to normal values for that specific activator. Just as this is done with PT or partial thromboplastin time PTT testing, this needs to be done with TEG measurements. It is also important for providers who are interpreting TEG results to understand how different activators can influence the results of different hemostatic agents (23). Pediatric values from 28 weeks gestation have been reported to be equal to adult values (24).

The initial TEG results of our patient showed a decreased R-time, prolonged K-time, and decreased MA and G-value. These results combined with the patient's severe hemodynamic instability indicated that plasma, cryoprecipitate, platelets, and rFVIIa were needed based on the algorithm developed and utilized by the by trauma service at Wilford Hall Trauma Center for the past 3 years (Table 3). The pattern of shortened R-time and prolonged K-time is often seen in patients with traumatic injury after resuscitation with crystalloids, and is possibly explained by the effect of hemodilution on R-time (25). This may be explained by a relative decrease in anti-thrombin III concentrations as a result of the mild to moderate hemodilution (26) or may be a result of procoagulant effects secondary to the proinflammatory effects of crystalloid infusions (27, 28). Therefore, in the patient we present, the pattern of a short R-time and lengthened K-time, reduced MA and G-value is consistent with mild to moderate hemodilution and coagulopathy secondary to trauma that required the administration of clotting factors, fibrinogen, and platelets. Increased factor and platelet interactions from pharmacologic dosing of rFVIIa may have provided an additional benefit (29). This effect further supports our use of rFVIIa with life-threatening bleeding for patients with increased K-times in our Wilford Hall Trauma Center algorithm despite the shortened R-time. The use of rFVIIa for patients with traumatic injuries is controversial due to the concern for increased thrombotic risks. A prospective randomized controlled trial in adult patients with blunt trauma (30), did not indicate increased thrombotic risk with rFVIIa use, but did reveal that rFVIIa use

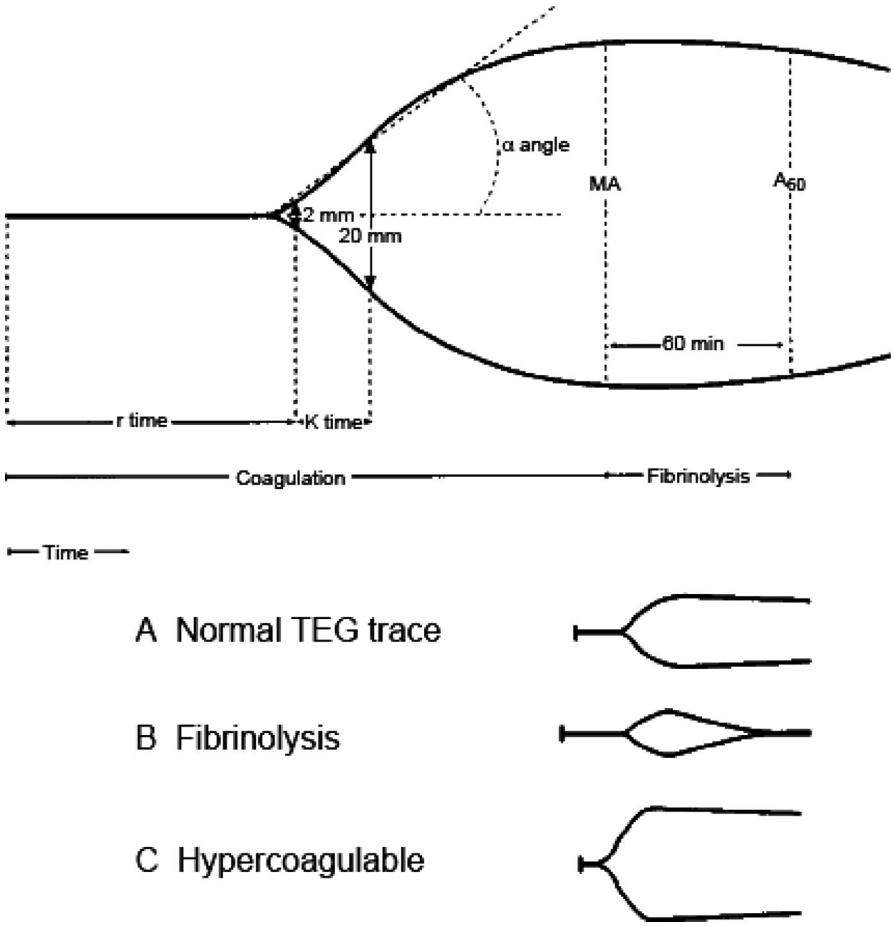

Figure 1. TEG tracing parameters and representative curves for hemostatic states. *MA*, maximum amplitude; *TEG*, thromboelastography.

Table 3. Primary and secondary treatment options for TEG directed haemostatic resuscitation for children with traumatic injuries and significant bleeding

Abnormal TEG Value[a]	Primary Treatment	Secondary Treatment
R-time		
8–10 min	FFP (10 mL/kg)	
10–14 min	FFP (15 mL/kg)	rFVIIa (90 μg/kg)[b]
>14 min	FFP (20 mL/kg)	rFVIIa (120 μg/kg)[b]
K-time		
>4 min	Cryoprecipitate (0.1 units/kg)	FFP (10–15 mL/kg); rFVIIa (90 μg/kg)[b]
Alpha angle		
<45°	Cryoprecipitate (0.1 units/kg)	FFP (10–15 mL/kg); rFVIIa (90 μg/kg)[b]
Maximum amplitude		
49 mm–54 mm	DDAVP (0.3 μg/kg) or apheresis platelets (10 mL/kg)	
40 mm–48 mm	Apheresis platelets (10 mL/kg)	Cryoprecipitate (0.1 units/kg)
<40 mm	Apheresis platelets (15–20 mL/kg)	Cryoprecipitate (0.1 units/kg)
Lysis at 30 min		
>7.5% and G <6	Consider Amicar (200 mg/kg IV)	

TEG, thromboelastography; FFP, fresh frozen plasma; rFVIIa, recombinant activated factor VII; DDAVP, desmopressin acetate.

[a]Abnormal values reported for kaolin activated samples. Secondary treatment may be given with primary treatment if immediate life threatening injury; [b]the use of rFVIIa should be reserved for life-threatening bleeding only. If bleeding not resolved clinically repeat TEG 30 min after treatment given.

was associated with decreased acute respiratory distress syndrome. Studies large enough to evaluate its effect on survival have not been completed.

Recently, the advantages of TEG compared with standard laboratory analysis of coagulation in accurately assessing the coagulation status of patients, and to determine the efficacy of rFVIIa, have been discussed (12, 21, 22). A major advantage of TEG is that it rapidly provides a qualitative or functional measurement of the entire coagulation cascade at the patient's temperature. TEG utilizes whole blood and therefore is able to asses the interaction between coagulation factors and platelets. Abnormalities in R and K times and alpha-angle can be determined within 10 minutes of sampling, which can be used to determine whether fresh frozen plasma, cryoprecipitate, platelets, or rFVIIa is indicated. The use of TEG to direct the use of hemostatic agents is not limited to rFVIIa and can be applied to other agents such as factor eight inhibitor by-passing activity.

Additionally, TEG is the only readily available method to accurately assess the fibrinolytic system (31). Studies in adults indicate that 20% of severe trauma patients have hyperfibrinolysis (16). The potential for TEG to determine which patients would benefit from antifibrinolytic therapies is currently being explored (32).

TEG can also be used to either indicate or exclude the use of rFVIIa. Most patients with trauma are hypercoaguable (12). TEG can identify a hypercoaguable state (short R- and K-time with increased alpha angle, MA, or G) and prevent the inappropriate use of hemostatic agents such as rFVIIa (12, 21). TEG also provides objective data that can be interpreted to determine whether more coagulation factors or platelet activation is needed for thrombin generation and clot strength. If coagulation factors are deficient (prolonged R-time), thrombin generation is decreased (prolonged K-time, decreased alpha angle) or clot strength is weak (low MA) then rFVIIa is potentially indicated (Table 3), as long as there is adequate fibrinogen and platelet function, which can also be assessed by TEG.

If the transfusion of blood products had been conducted by the classic approach, which utilizes standard laboratory analysis to guide resuscitation, plasma administration may have been delayed while waiting for PT results (the PT was reported 50 minutes after TEG results in the operating room) and platelets and cryoprecipitate may not have been transfused (Table 1). Compared with empirical formulas, TEG directs and confirms which specific products are needed to optimize coagulation. Recent review articles have suggested an approach termed "damage control resuscitation," (or alternatively, "hemostatic resuscita-

tion"), for patients who present with the coagulopathy of trauma. This is described as rapid surgical control of bleeding with the transfusion of a 1:1:1 ratio of plasma: RBCs: platelets, with the early administration of cryoprecipitate, rFVIIa, and with an emphasis on decreased use of crystalloid solutions (5). Retrospective studies have associated this approach with improved survival in patients with severe traumatic injury (8), including a retrospective report that associated the early use of rFVIIa in patients with severe penetrating trauma with improved 30-day survival (9). The importance of rapid treatment and correction of the coagulopathy of trauma is highlighted by the evidence that the majority of patients with severe trauma and massive transfusion who die do so within 6 hours. TEG has the potential to augment damage control resuscitation by providing rapid assessment of coagulation deficits that will aid in the administration and titration of prohemostatic products such as platelets, fibrinogen in the form of cryoprecipitate, and rFVIIa. In addition, the rapid and targeted correction of coagulopathy may minimize the use of crystalloids and RBCs, which is advantageous since excessive use of crystalloids and RBCs have both been associated with increased risk of morbidity and mortality (14, 27, 33, 34).

Limitations of TEG include the need for dedicated personnel to run the test as well as initial education of providers in the interpretation of TEG values. TEG measures the function of hemostasis and does not directly quantitatively measure individual factors, fibrinogen, or platelets. Whether TEG decreases blood product utilization or improves outcomes in children or adults with traumatic injuries is currently unknown. The algorithm we utilize and describe in this report has not been validated to decrease blood product transfusion or to improve clinical outcomes.

CONCLUSIONS

TEG has the potential to be an effective method to rapidly direct hemostatic resuscitation in patients with the coagulopathy of trauma. TEG is a quick and focused method of qualitatively assessing the entire coagulation cascade from clot formation to fibrinolysis and can be used to guide a targeted transfusion approach to the treatment of coagulopathy. Prospective studies that evaluate the ability of TEG to decrease transfusion requirements and improve morbidity and mortality outcomes in children with traumatic injuries are needed.

REFERENCES

1. Sauaia A, Moore FA, Moore EE, et al: Epidemiology of trauma deaths: A reassessment. *J Trauma* 1995; 38:185–193
2. Krug EG, Sharma GK, Lozano R: The global burden of injuries. *Am J Public Health* 2000; 90:523–526
3. Brohi K, Singh J, Heron M, et al: Acute traumatic coagulopathy. *J Trauma* 2003; 54: 1127–1130
4. Como JJ, Dutton RP, Scalea TM, et al: Blood transfusion rates in the care of acute trauma. *Transfusion* 2004; 44:809–813
5. McMullin NR, Holcomb JB, Sondeen J: Hemostatic Resuscitation. *In:* Yearbook of Intensive Care and Emergency Medicine. Vincent J, (Ed). New York, Springer, 2006, pp 265–278
6. Stewart RM, Myers JG, Dent DL, et al: Seven hundred fifty-three consecutive deaths in a level I trauma center: The argument for injury prevention. *J Trauma* 2003; 54:66–70; discussion 70–61
7. Deleted in proof
8. Borgman MA, Spinella PC, Perkins JG, et al: The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. *J Trauma* 2007; 63:805–813
9. Spinella PC, Perkins JG, McLaughlin DF, et al: The effect of recombinant activated factor VII on mortality in combat-related casualties with severe trauma and massive transfusion. *J Trauma* 2008; 64:286–293; discussion 293–284
10. Shore-Lesserson L, Manspeizer HE, DePerio M, et al: Thromboelastography-guided transfusion algorithm reduces transfusions in complex cardiac surgery. *Anesth Analg* 1999; 88:312–319
11. Srinivasa V, Gilbertson LI, Bhavani-Shankar K: Thromboelastography: Where is it and where is it heading? *Int Anesthesiol Clin* 2001; 39:35–49
12. Kaufmann CR, Dwyer KM, Crews JD, et al: Usefulness of thrombelastography in assessment of trauma patient coagulation. *J Trauma* 1997; 42:716–720; discussion 720–712
13. Goodman AM, Pollack MM, Patel KM, et al: Pediatric red blood cell transfusions increase resource use. *J Pediatr* 2003; 142:123–127
14. Kneyber MC, Hersi MI, Twisk JW, et al: Red blood cell transfusion in critically ill children is independently associated with increased mortality. *Intensive Care Med* 2007; 33:1414–1422
15. Trowbridge CC, Stammers AH, Ciccarelli N, et al: Dose titration of recombinant factor VIIa using thromboelastograph monitoring in a child with hemophilia and high titer inhibitors to factor VIII: A case report and brief review. *J Extra Corpor Technol* 2006; 38:254–259
16. Martinowitz U, Michaelson M: Guidelines for the use of recombinant activated factor VII (rFVIIa) in uncontrolled bleeding: A report by the Israeli Multidisciplinary rFVIIa Task Force. *J Thromb Haemost* 2005; 3:640–648
17. Sorensen B, Ingerslev J: Tailoring haemostatic treatment to patient requirements—An update on monitoring haemostatic response using thrombelastography. *Haemophilia* 2005; 11(Suppl 1):1–6
18. Salooja N, Perry DJ: Thrombelastography. *Blood Coagul Fibrinolysis* 2001; 12:327–337
19. Attar S, Boyd D, Layne E, et al: Alterations in coagulation and fibrinolytic mechanisms in acute trauma. *J Trauma* 1969; 9:939–965
20. Sorensen B, Ingerslev J: Thromboelastography and recombinant factor VIIa-hemophilia and beyond. *Semin Hematol* 2004; 41(Suppl 1):140–144
21. Schreiber MA: Coagulopathy in the trauma patient. *Curr Opin Crit Care* 2005; 11:590–597
22. Hendriks HG, Meijer K, de Wolf JT, et al: Effects of recombinant activated factor VII on coagulation measured by thromboelastography in liver transplantation. *Blood Coagul Fibrinolysis* 2002; 13:309–313
23. Avidan MS, Da Fonseca J, Parmar K, et al: The effects of aprotinin on thromboelastography with three different activators. *Anesthesiology* 2001; 95:1169–1174
24. Miller BE, Tosone SR, Guzzetta NA, et al: Fibrinogen in children undergoing cardiac surgery: Is it effective? *Anesth Analg* 2004; 99:1341–1346; table of contents
25. Jamnicki M, Zollinger A, Seifert B, et al: Compromised blood coagulation: An in vitro comparison of hydroxyethyl starch 130/0.4 and hydroxyethyl starch 200/0.5 using thrombelastography. *Anesth Analg* 1998; 87:989–993
26. Nielsen VG, Lyerly RT III, Gurley WQ: The effect of dilution on plasma coagulation kinetics determined by thrombelastography is dependent on antithrombin activity and mode of activation. *Anesth Analg* 2004; 99: 1587–1592, table of contents
27. Cotton BA, Guy JS, Morris JA Jr, et al: The cellular, metabolic, and systemic consequences of aggressive fluid resuscitation strategies. *Shock* 2006; 26:115–121
28. Levi M, van der Poll T: Two-way interactions between inflammation and coagulation. *Trends Cardiovasc Med* 2005; 15:254–259
29. Hoffman M: A cell-based model of coagulation and the role of factor VIIa. *Blood Rev* 2003; 17(Suppl 1):S1–S5
30. Boffard KD, Riou B, Warren B, et al: Recombinant factor VIIa as adjunctive therapy for bleeding control in severely injured trauma patients: Two parallel randomized, placebo-controlled, double-blind clinical trials. *J Trauma* 2005; 59: 8–15; discussion 15–18
31. Yamakage M, Tsujiguchi N, Kohro S, et al: The usefulness of celite-activated thromboelastography for evaluation of fibrinolysis. *Can J Anaesth* 1998; 45:993–996
32. Fries D, Haas T, Salchner V, et al: [Management of coagulation after multiple trauma]. *Anaesthesist* 2005; 54:137–144
33. Napolitano LM, Corwin HL: Efficacy of red blood cell transfusion in the critically ill. *Crit Care Clin* 2004; 20:255–268
34. Spinella PC, Perkins JG, Grathwohl KW, et al: Risks associated with fresh whole blood and red blood cell transfusions in a combat support hospital. *Crit Care Med* 2007; 35:2576–2581